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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,235	03/19/2001	Seishi Kato	GIN-6715CPUS	3254

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,235	KATO ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-3 and 5-10 are pending in the instant application. Claims 1-3, 5 and 6 have been amended, claim 4 has been canceled and claims 7-10 have been added as requested by Applicant in Paper Number 11, filed November 22, 2002.

Withdrawn Objections and Rejections

2. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Claim Objections

3. Claims 3 and 5 are objected to because of the following informalities:

3.1 Claim 3 is also objected to because the first "sequence" should be the plural form "sequences" to correlate with the rest of the claim.

3.2 Claim 5 is objected to because the word "express" should be "expression", which was recited in the pre-amended claim.

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial utility or a well established utility, for reasons cited in the previous Office Action, Paper No. 9, at pages 3-8, and for the reasons below.

Applicants traverse the rejection and assert that they believe that that protein is sufficiently similar to rat organic cation transporter (67.5% homology at the N-terminal 169 amino acid portion) that it evidences similar drug excretion-associated activity. Applicants cite Principles of Protein Structure, Cantor ed., and assert that the art is evidence that establishing homology between the unknown and reference proteins permits the skilled artisan to assume the unknown unexpressed protein and the known reference protein have the same function. Applicants also cite Example 10 of the Utility Training Materials, and point out that in that example, the Examiner is directed not to reject claims merely because the Applicant's asserted utility is premised on the "overall level of sequence similarity between the unknown sequence and the consensus of the known DNA ligases that are presented in the specification. Applicants also assert that the guidelines do not require a minimum percentage required to determine function from homology. Applicants also point out on page 6 of the amendment that the Federal Circuit acknowledges that "utility is well-established if it is apparent to one skilled in the art ("genus claims to nucleic acids based on their hybridization properties....[if the subject matter of the claims will] hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar.")".

Applicants' arguments have been fully considered but are not deemed persuasive. Although the guidelines do not require a minimum percentage required to determine function from homology, the number of proteins having homology, and the degree of homology of those

proteins, are also taken into account when determining when the amount of homology is sufficient to assume that an unknown protein is likely to have the same function as that of known proteins. While it is true that sequence similarity can be used to predict function, the extent of the sequence similarity and the families of proteins are also important considerations when predicting similar function. Example 10 of the Training materials deals with a nucleic acid encoding a protein that has an overall sequence similarity of 95% to the consensus sequence of known DNA ligases. This is a very high sequence similarity and differs greatly from the degree of homology between the protein of the instant invention and the proteins of rat, mouse and human (previous Office Action, page 5). Additionally, Example 10 also states that the next highest level of homology of the unknown protein, which is 50%, is to alpha-actin, a completely difference type of protein, and that based on the sequence similarities, the unknown protein is classed with the DNA ligases and not alpha-actin. So while sequence similarity can often be used to predict function and place proteins in classes, the degree of sequence similarity is a significant consideration as well as the type of protein. Additionally, while a gene that hybridizes under highly stringent conditions to genes encoding proteins with known activity would be evidence that the unknown gene encodes a protein having similar activity, again the degree of hybridization would be taken into account. Genes that hybridize under highly stringent conditions are analogous to proteins having 95% sequence similarity, which is not the same as the instant situation.

It is not disputed that the protein of the instant invention and that of the rat (and human) organic cation transporter are related. However, the divergence in both overall protein structure and amino acid mismatches of the protein of the instant invention and those makes it likely that

the protein of the instant invention is either an inactive pseudogene, or has an activity different from that of the other proteins. The protein of the instant invention is only 268 amino acids in length, and contains only two transmembrane domains as opposed to the eleven transmembrane domains of the most homologous proteins of rat, mouse and human (previous Office Action, page 5). The human protein of Suzuki et al., database SPTREMBL_19, Accession No. Q96LX3, is 55% identical to the protein of the instant invention, but this protein is 552 amino acids in length, and contains an additional 108 amino acids inserted between amino acids 168 and 169. Additionally, over the 249 amino acids in the alignment, 93 amino acids are mismatches. A similar protein from mus musculus, (Strausberg, R., database SPTREMBL_19, Accession No. Q91WJ2, Dec. 1, 2001) is 53.4% identical to the protein of the instant invention, but the mus musculus protein is also 552 amino acids in length. Additionally, all of these proteins contain an additional approximately 108 amino acids inserted between amino acids 168 and 169 of the protein of SEQ ID NO: 1 (see sequence alignments). Given the significant differences in structure between the rat, mouse and the other human protein, and especially in light of the fact that the human protein disclosed by Suzuki et al. is much more similar to the rat and mouse proteins than to the human protein disclosed in the instant application, one of ordinary skill in the art would not conclude that the protein of the instant invention would function in the same manner as the other proteins, if it actually does have a function. Given the dissimilarities in structure, it is possible that the protein of the instant invention is a pseudogene of the cation transporters. Benjamin Lewin, Editor, GENES, John Wiley and Sons, pages 337 and 350, teach that pseudogenes are related to the genes from which they derived and often have the same general structure, and the earlier the pseudogene originated, the more mutations start to

accumulate. Comparing the sequence of the protein of the instant invention with those of the cation transporters, demonstrates the significant differences in both secondary structure (the number of transmembrane domains) and overall amino acid sequence.

Applicants on page 6 of the amendment also point out that, at the very least, the resemblance of the present invention to specific proteins of known activity makes it clear the present invention can be further utilized as research tools for better characterizing those prior art compounds, that this is a specific utility, and specific utility does not exclude even generalized research tools like probes, when the target being probed is already known (Revised Interim Utility Guidelines Training Materials at pages 50-53, and Federal Circuit Bar Journal, Vol. 11, No. 4 (2002) 918).

Applicants' arguments have been fully considered but are not deemed persuasive. The example at pages 50-53 of The Revised Interim Utility Guidelines Training Materials teach that use of either full-length cDNA's encoding proteins of unknown function or fragments of those cDNA's do not have a specific, substantial or well-established utility.

Therefore, for the reasons discussed in the previous Office Action and those above, the rejection is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-3 and 5-10 also remain rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with

regard to the rejection of these claims under 35 U.S.C. § 101, and for reasons in the Previous Office Action, Paper No. 9.

It is believed that all pertinent arguments have been answered.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 3 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6.1 Claim 3 is indefinite because the word "any" is inclusive, and one or both SEQ ID NOS. are encompassed. It is suggested that the word "any" be replaced by "either".

6.2 Claim 5 is indefinite because the claim language is confusing. As written, the claim reads as "an expression vector that expresses the DNA by transformation". It is suggested the claim be amended to replace "transformation in" with "by transformed".

Conclusion

7. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

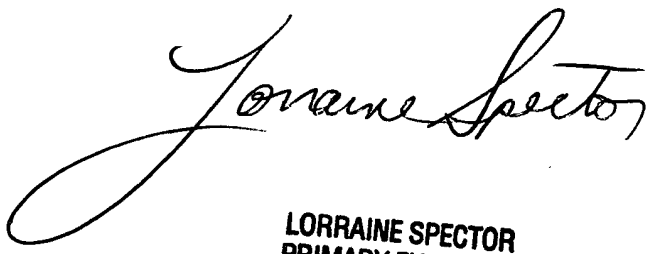
Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner



LORRAINE SPECTOR
PRIMARY EXAMINER